REMARKS

I. Claim Status

Claims 1-10 and 12-15 are currently pending. Claim 11 has been canceled without prejudice herein, and claims 9 and 12-15 have been withdrawn. Claims 1-10 and 12-15 have been amended herein. Those amendments are supported in the original specification and claims. Accordingly, no new matter is added.

II. Restriction Requirement

Applicants wish to clarify the record with respect to the Examiner's discussion surrounding the Restriction Requirement. In particular, the Examiner indicates that "Unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. 371." Office Action at 3. Applicants agree with that statement, but disagree with the Examiner's classification of this application as one filed under 35 U.S.C. 111(a): "Consequently, the checking of box IV of the PCT written opinion has no bearing on examination practices in the U.S." *Id.* This application is, in fact, a national stage application submitted under § 371. Accordingly, Unity of Invention practice does apply.

Applicants maintain their arguments regarding the required restriction but acknowledge the finality thereof.

III. Claim Rejections

Enablement Rejection

Claim 3 has been rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. Office Action at 4. Applicants respectfully traverse this rejection.

Although the Examiner concedes that the specification is enabling for "a method of treating one or more withdrawal symptoms caused by the discontinuation of the use of at least one psychostimulant . . . which comprises administering to the mammal an effective amount of a selective alpha-2-adrenocepter antagonist," she contends that the specification "does not reasonably provide enablement for a method to prevent the aforementioned conditions." *Id.* In support of this rejection, the Examiner points to a review article by Murray, "Psychophysiological Aspects of Amphetamine-Methamphetamine Abuse," *J. Psych.* (1998) 132(2):227-237 ("Murray"), which discloses an overview of amphetamine and methamphetamine abuse, related research, and psychotherapeutic strategies,[1] concluding without providing a reason why "prevention of withdrawal symptoms regardless of the severity is unlikely." Office Action at 4.

Applicants respectfully point out that the Examiner has the burden to provide a reason for why the specification lacks an enabling disclosure. In fact, if "a specification disclosure contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented," the Examiner must accept that specification as being in compliance with the enablement requirement "unless there is a reason to doubt the objective truth of the statements contained therein." *See* M.P.E.P. § 2164.04. Applicants assert that the present specification recites a process of making and using

[1] The Examiner asserts that Murray discloses that chronic drug abusers develop withdrawal symptoms at p. 231, para. 3. Applicants respectfully point out that that paragraph refers to the effects of the drug itself, i.e., paranoia, and not a withdrawal symptom of that drug. Accordingly, the Examiner's citation has no bearing on the whether the present specification is enabling.

an invention within the scope of the present claims, and that the Examiner's conclusory statements do not substantiate a *prima facie* case of non-enablement.

The present specification discloses that "selective alpha2-adrenoceptor antagonist, atipamezole [] produced cue can be substituted by the psychostimulants d-amphetamine and cocaine . . . in rats . . . [and thus] can be used for ***prevention*** and treatment of physical dependence and withdrawal symptoms caused by the subacute use . . . of psychostimulant." Specification at 4 (emphasis added). One of skill in the art based on the present disclosure would know how to make and use the present invention because the "drug discrimination (generalization) approach has been widely utilized to determine if a drug-induced stimulus will substitute for other drugs of a specific class . . . ," i.e., can be used to treat and/or prevent the symptoms of drug dependence and withdrawal. *Id.* at 1. Because Applicants disclose a working example of the drug discrimination approach, showing that selective alpha2-adrenoceptor antagonists, atipamezole and MPV-1730 HCl, can generalize amphetamine and cocaine, representative stimulants, one of skill in the art would know how to practice the invention according to the present claims without undue experimentation. In addition, the present specification includes guidance regarding the dosage range and modes of administration, as well as the time period for when the prevention may occur. Specification at 5, lines 24-32 and page 9, lines 29-32.

In addition, Applicants wish to clarify the Examiner's definition of "prevention." Applicants agree with the Webster's definition that "prevention" means "to keep from happening or existing." However, Applicants disagree that "prevention" is synonymous with "eradication." According to Webster.com "eradicate" is defined as

> 1 : to pull up by the roots
>
> 2 : to do away with as completely as if by pulling up by the roots.

(definition submitted herewith)

Accordingly, "eradication" relates to removing something that is already present, and does not mean to keep something from happening. In contrast to the Examiner's contention that under the present claims, "complete eradication of [the symptoms]" is necessary, Applicants assert that the present claims indicate that ***one or more*** of the symptoms will be treated and/or prevented. The present claims do not require complete treatment and/or prevention of ***all*** of the symptoms of withdrawal.

For at least these reasons, this rejection should be withdrawn.

102(b) Rejection

Claims 1-2 and 6-8 are rejected under 35 U.S.C. § 102(b)[2] as being anticipated by U.S. Patent No. 7,012,085 to Seiler et al. ("Seiler") as evidenced by Murray. Office Action at 7. Applicants respectfully traverse this rejection.

Without in any conceding the propriety of the rejection and solely in an effort to expedite prosecution, Applicants have amended claim 1 herein to read

> . . . comprising administering to the mammal an effective amount of a selective alpha2-adrenoceptor antagonist chosen from atipamezole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole, 4-(2-ethyl-5,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole, and their pharmaceutically acceptable salts.

[2] Applicants respectfully point out that Seiler is not 102(b) prior art to the present application. Instead Seiler is either 102(a) art based on the international application's WO 01/55132 publication date or 102(e) based on the international application's filing date.

Those recited alpha2-adrenoceptor antagonists are not disclosed in either Seiler or Murray. Accordingly, Seiler as evidenced by Murray does not anticipate the present claims. For at least this reason, this rejection should be withdrawn.

103(a) Rejections

Claims 1-2 and 6-8 have been rejected under 35 U.S.C. § 103(a) as being obvious over Seiler in view of Murray. Office Action at 8. Applicants respectfully traverse this rejection.

As discussed above, the Seiler and Murray disclosures do not anticipate the presently pending claims. Seiler in combination with Murray does not render the present claims obvious. Seiler discloses structurally and arguably functionally different alpha-2-adrenoceptor antagonists. For example, the compounds of Seiler show "high affinity at α_2 adrenoceptor subtypes, with selectivity to α_{2C}." Those compounds also have effects on serotinergic and dopaminergic systems, whereas the ***selective*** alpha2-adrenoceptor antagonists of the present claims do not affect those systems and are, as a result, devoid of side effects associated with them. *See* Specification at 2, line 30-page 3, line 2 and page 6, lines 11-22.

Even though drug abuse is contemplated among a list of different potential therapeutic targets, the Seiler disclosure points to the treatment of schizophrenia and depression as preferred embodiments. *See* col. 4, lines 7-15, 55-56. In contrast, atipamezole has been show to be ineffective in a rat depression model. *See generally*, Kauppila, T., et al. "Effects of atipamezole, a novel alpha2-adrenoceptor antagonist, in open-filed, plus-maze, two compartment exploratory, and forced swimming tests in the rat," *Eur. J. Pharmacol.* (1991) 205(2):177-182 (submitted herewith). Consequently,

one of skill in the art would have no reason to modify the teaching of Seiler to arrive at the present claims based on its disclosure and the knowledge in the art at the time of the invention.

Murray, which discloses that withdrawal symptoms occur, does not compensate for any of Seiler's deficiencies. Accordingly, a *prima facie* case of obviousness has not been established. Therefore, this rejection should be withdrawn.

Claim 10 has been rejected under 35 U.S.C. § 103(a) as being obvious over Seiler in view of Murray and further in view of Sallinen et al. (*J. Neuroscience* (1998) 18(8):3035-3042, "Sallinen"). Office Action at 11. Applicants respectfully traverse this rejection.

As discussed above, Seiler and Murray do not render obvious the present claims. Applicants assert that not only does Sallinen not compensate for their deficiencies, it also teaches away from the present claims. In particular, Sallinen discloses the results using mice models of underexpressed and overexpressed α_{2C} adrenoceptors. The Examiner asserts that Sallinen "teaches the use of atipamzole for drug withdrawal symptoms." However, Sallinen discloses using atipamezole as a ***subtype nonselective*** antagonist and provides the speculative statement that "drugs acting via α_{2C}-ARs might have therapeutic value in disorders associated with enhanced startle responses and sensorimotor gating deficits, such as . . . drug withdrawal." *See* Abstract and page 3041, second col. In other words, Sallinen discloses that ***subtype-selective*** α_{2C}-ARs might have therapeutic value for drug withdrawal symptoms. Accordingly, one of skill in the art would have no reason to expect success when treating drug withdrawal symptoms with a subtype non-selective antagonist according to

the presently pending claims. For at least that reason, Seiler in view of Murray further in view of Sallinen does not render the present claim obvious. Accordingly, this rejection should be withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: June 18, 2008

By: Erin M. Sommers
Erin M. Sommers
Reg. No. 60,974

eradicate

One entry found.

eradicate

Main Entry: **erad·i·cate**
Pronunciation: \i-'ra-də-,kāt\
Function: *transitive verb*
Inflected Form(s): **erad·i·cat·ed; erad·i·cat·ing**
Etymology: Latin *eradicatus*, past participle of *eradicare*, from *e-* + *radic-*, *radix* root — more at ROOT
Date: 1532

1 : to pull up by the roots
2 : to do away with as completely as if by pulling up by the roots <programs to *eradicate* illiteracy>

synonyms see EXTERMINATE
— **erad·i·ca·ble** \-'ra-di-kə-bəl\ *adjective*
— **erad·i·ca·tion** \-,ra-də-'kā-shən\ *noun*
— **erad·i·ca·tor** \-,kā-tər\ *noun*

Learn more about "eradicate" and related topics at Britannica.com

Find Jobs in Your City

Pronunciation Symbols